# Deep brain stimulation to reduce sexual drive

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To date there are few treatment options to reduce high sexual drive or sexual urges in paraphilic patients with a risk for sexual offending. Pharmacological therapy aims to reduce sexual drive by lowering testosterone at the cost of severe side effects. We hypothesize that high sexual drive could also be reduced with deep brain stimulation (DBS) of circuits that generate sexual drive. This approach would help to avoid systemic side effects of antiandrogenic drug therapies. So far the best investigated target to reduce sexual drive is the ventromedial hypothalamus, which was lesioned unilaterally and bilaterally by stereotaxic interventions in paraphilic patients in the 1970s. Here, we discuss DBS as a treatment strategy in patients with severe paraphilic disorders with a serious risk of sexual offending. There are profound ethical and practical issues associated with DBS treatment of paraphilic patients that must be solved before considering such a treatment approach.

Currently, reduction of sexual drive in patients with psychiatric disorders can be achieved with antihormonal pharmacotherapy (medroxyprogesterone acetate, antiandrogen cyproterone acetate, GnRH agonists), selective serotonin reuptake inhibitors (SSRIs) and cognitive behavioural therapy.[1] Although solid evidence is lacking for antihormonal treatment,[2] some countries decide by verdict to treat sex offenders with antihormonal therapy in order to reduce the risk for reoffending.[3] Large meta-analyses have suggested that antihormonal therapy reduces recidivism rates in sexual offenders.[4,5] Therefore the World Federation of Societies of Biological Psychiatry has suggested guidelines for the biological treatment of paraphilias, including antihormonal and SSRI treatment.[6]

In addition to sexual offenders, paraphilic and hypersexual patients who have never shown delinquent behaviour and experience severe distress from recurrent sexual urges demand antihormonal therapy.[7] The sexual urges of these patients are linked to qualitative (e.g., pedophilic sexual interest) and/or quantitative (hypersexual, compulsive or addictive) abnormalities, and they seek medical assistance in hopes of overcoming or at least controlling sexual urges that could bring them into conflict with society and the law or that impair their social and occupational functioning. Treatment of these patients and of sex offenders, however, raises thorny ethical problems because potential harm to a third person (e.g., in sexual sadism or pedophilic disorder) has to be considered. The meager evidence for these treatments further complicates ethical concerns; a first double-blind controlled clinical trial for antihormonal treatment is only in the planning stages.[8] Moreover, patients have to accept severe side effects like osteoporosis, mood disturbances and increased risk for thromboembolic complication as well as cerebrovascular and cardiovascular diseases that can be associated with antihormonal treatment.[9] Thibaut and colleagues[6] therefore suggested ethical standards for the indication of antihormonal therapy.

A targeted therapy that reduces sexual drive specifically without the systemic hormonal disturbances of antiandrogens would be desirable. While it seems unlikely that biological therapy would target the appearance of distinct paraphilic thoughts in the brain, neural circuits that generate sexual drive could be identified and inhibition of these circuits might lead to a reduction of sexual urge and hence relieve patients and open new venues for psychotherapy.

With the advent of deep brain stimulation (DBS) to treat a number of psychiatric disorders (targeting, for example, depressive or compulsive symptoms) we also suggest sexual drive as a potential target for DBS. Brain areas that are associated with sexual arousal have been repeatedly identified, and these may be discussed as targets for DBS (for a review see Mohnke and colleagues[10] and for a recent meta-analysis see Kühn and Gallinat[11]). However, based on experiences with earlier stereotaxic brain lesions, the best evidence exists for the inhibition of the ventromedial hypothalamus.

From 1962 to the late 1970s a considerable number of people in Germany received stereotaxic brain lesions to treat paraphilic sexual desires (e.g., pedophilic disorder and exhibitionism). Most prominent was the unilateral lesion of the ventromedial hypothalamus. Results were published in case series

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and promised remarkable effects that induced a reduction of sexual drive with fewer side effects than pharmacological treatment with antiandrogens.[12] Roeder and colleagues[12] conducted a case series of 10 patients; 9 received unilateral stereotaxic ablation of the ventromedial hypothalamic nucleus (Cajal) and 1 received bilateral lesions. From today's perspective, however, only half of these patients would have been considered to have a paraphilic disorder ($n$ = 4 patients with pedophilic disorder). The others were homosexual, which in those days was considered to be a psychiatric diagnosis; homosexuality was deleted from the *Diagnostic and Statistical Manual of Mental Disorders* in 1973. Irrespective of the diagnosis, it was reported that stereotaxic lesion of the ventromedial hypothalamus reduced sexual drive remarkably.[12,13] Subsequently, 75 people (74 men, 1 woman) were documented to have been treated with ventromedial hypothalamotomy in Germany.[13] However, Bernd Lichtenberg, who had been operated in Hamburg in 1976, killed a 10-year-old boy 3 years later.[14] Subsequently, psychosurgery of sex offenders became a major political topic in Germany and was profoundly criticized[13,15] and finally abandoned. Unfortunately, a systematic follow-up examination of the operated individuals was never published in a scientific peer-reviewed journal. Schmidt and Schorsch[13] reported that initial endocrinological disturbances after the operation normalized after 6–10 months but that weight gain lasted in most patients. Hebestreit[16] completed a dissertation in 1989 about psychological examinations before and after hypothalamotomy and reported that patients operated in Hamburg exhibited no neurocognitive deficits after surgery. Timmann and Müller[17] self-published a book in 2003 after interviewing 26 of the operated individuals many years after surgery and reported that long-term follow-up and satisfaction of these individuals was surprisingly good. These 2 publications[16,17] never underwent a formal peer review, however, and cannot be interpreted as evidence-based.

In contrast to other psychosurgical interventions in which brain lesions had volumes up to 15 $cm^3$, the ventromedial hypothalamotomy lesioned an area of only 80 $mm^3$. As a phyllogenetically old brain structure, the ventromedial hypothalamus is present in mice and men. Two major publications have recently highlighted the role of the murine ventromedial hypothalamus in male aggression and sexual behaviour.[18,19] Lin and colleagues[18] demonstrated that acute optogenetic stimulation of neurons in the ventrolateral subdivision of the ventromedial hypothalamus induced aggression in male mice. Stimulation led to attacks toward an intruder. The fighting ceased when the stimulation stopped. The authors also identified cells in the same brain region that were active during mating and that were distinct from the neurons that were active during fighting. Yang and colleagues[19] genetically ablated neurons that carried a progesterone receptor (roughly 50%) within the same ventrolateral division of the ventromedial hypothalamus of male mice. Chronic ablation of these neurons significantly reduced mating behaviour and aggression. Interestingly, sex discrimination, emotional behaviours and territory marking were not affected. These recent studies indicate that acute activation of neurons in the ventromedial hypothalamus induces aggression in male mice and chronic inhibition reduces aggression and mating behaviour, confirming the assumption that the ventromedial hypothalamus is involved in the generation of sexual behaviour and that its function may correlate with sexual drive. A recent meta-analysis of human brain response to sexual stimuli found an activation of the hypothalamus.[11]

With the advent of DBS to treat a number of psychiatric disorders, sexual drive may be discussed as a possible therapeutic target for DBS. Compared with psychosurgical procedures, DBS is less destructive but rather reversible and more adjustable to the clinical symptoms and side effects. Small case series of DBS in the posterior hypothalamus to reduce aggressive behaviour have been performed successfully.[20,21] However, DBS in paraphilic patients will exceedingly touch sensitive practical and even more ethical issues. Especially with regard to experiences in Germany with psychosurgical intervention in patients with deviant sexual behaviour without sufficient proof of efficacy and the history of involuntary castration of sex offenders,[22] it is extremely important that future studies should comply with rigorous scientific assessment and great ethical caution. The indication for DBS has to accrue from severe psychological strain, but on the other hand, appropriate candidates have to be capable of understanding risks and giving informed consent without any form of legal pressure. Mandatory DBS (as well as mandatory antiandrogen medication) should absolutely not be an option (for an ethical discussion of mandatory v. voluntary treatment of sexual offenders see Harrison[3]). Preferably, patients with paraphilic disorders (sexual sadism and pedophilia) who have uncontrollable sexual urges and a concomitant high risk for sexual offense[6] could eventually be eligible candidates. The treatment of these candidates should be openly debated to weigh ethical issues on an individual basis, as for example in the case of a sexual offender who demanded surgical castration after it had been abandoned in Europe.[23] The motivation for DBS treatment should not be connected to any hopes/promises of prematurely leaving prison or a forensic treatment facility as in the 1970s when most of the imprisoned sexual offenders were released after the operation. The boundary between treatment and punishment must be very clear. Thus, we propose that only those individuals who desire DBS treatment because they suffer from their sexuality to a high degree, have a high risk of severe sexual offending or in whom antiandrogens have been ineffective or have caused unacceptable side effects should be eligible for DBS. In any case, prosecuted sexual offenders could be eligible for DBS treatment only after it has been clearly demonstrated that DBS is superior to other treatments under certain conditions. But even with such a scientific proof of efficacy we would still face the problem that detained convicts may have a reduced capacity to give informed consent.[24]

A rigorous risk–benefit assessment would have to demonstrate that individual distress and risk surmounts the risk for side effects (e.g., intracerebral bleeding). Yet, even if suitable patients have been identified, a plethora of ethical and judicial questions would have to be considered: Is legal responsibility affected by DBS? Who is responsible if such a patient commits a sexual offense because the stimulator is not working properly? Who is allowed to reduce or stop the stimulation? What follow-up care is mandatory?

With our suggestions and concerns, we hope to stimulate a discussion to scrutinize these questions in more detail before anyone in the scientific community starts treating paraphilic patients with DBS. Stimulation might have fewer side effects than pharmacological therapies, as has been repeatedly demonstrated in patients with Parkinson disease.[25] However, consequences of a selective inhibition of sexual thoughts and urges are difficult to anticipate. Unexpected and undesirable personality changes have been reported following DBS in clinical practice.[26] These changes might unintentionally impede the individual's ability to gain control over paraphilic urges or even impair behavioural control.

Unlike in 1962 when paraphilic patients were treated without a prior scientific debate, now we must discuss ethical concerns and possible side effects before DBS treatment can be considered.

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## References

1. Assumpção AA, Garcia FD, Garcia HD, et al. Pharmacologic treatment of paraphilias. *Psychiatr Clin North Am* 2014;37:173-81.
2. Långström N, Enebrink P, Lauren EM, et al. Preventing sexual abusers of children from reoffending: systematic review of medical and psychological interventions. *BMJ* 2013;347:f4630.
3. Harrison K. Legal and ethical issues when using antiandrogenic pharmacotherapy with sex offenders. *Sex Offender Treatment* 2008;3.
4. Bradford JM, Fedoroff P, Gulati S. Can sexual offenders be treated? *Int J Law Psychiatry* 2013;36:235-40.
5. Losel F, Schmucker M. The effectiveness of treatment for sexual offenders: a comprehensive meta-analysis. *J Exp Criminol* 2005;1: 117-46.
6. Thibaut F, De La Barra F, Gordon H, et al. WFSBP Task Force on Sexual Disorders. The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of paraphilias. *World J Biol Psychiatry* 2010;11:604-55.
7. Turner D, Schöttle D, Bradford J, et al. Assessment methods and management of hypersexuality and paraphilic disorders. *Curr Opin Psychiatry* 2014;27:413-22.
8. Briken P, Berner W. Double-blind, controlled, clinical trial planned in Germany to investigate the efficacy of psychotherapy combined with triptorelin in adult male patients with severe pedophilic disorders: presentation of the study protocol. *Isr J Psychiatry Relat Sci* 2012;49:306-13.
9. Bradford JM. Organic treatment for the male sexual offender. *Ann N Y Acad Sci* 1988;528:193-202.
10. Mohnke S, Müller S, Amelung T, et al. Brain alterations in paedophilia: a critical review. *Prog Neurobiol* 2014;122:1-23.
11. Kühn S, Gallinat J. A quantitative meta-analysis on cue-induced male sexual arousal. *J Sex Med* 2011;8:2269-75.
12. Roeder F, Orthner H, Müller D. The stereotaxic treatment of pedophilic homosexuality and other sexual deviations. In: Hitchcock EL, L. Vaernet, K., editor. *Psychosurgery* Springfield: Charles C Thomas; 1972: 87–111.
13. Schmidt G, Schorsch E. Psychosurgery of sexually deviant patients: review and analysis of new empirical findings. *Arch Sex Behav* 1981;10:301-23.
14. Triebtäter in den Händen der Chirurgen. *Stern* 1979;32:12-9.
15. Sigusch V. Medizinische experimente am menschen: das beispiel psychochirurgie. Jahrbuch für kritische Medizin Beilage zum Argument Sonderband AS 1977; 17:1-31.
16. Hebestreit J. Testpsychologische befunde vor und nach stereotaktischer hypothalamotomie bei sexualstraftätern. Disseration at University of Hamburg 1989; 1-211.
17. Timmann HD, Müller D. Stereotaktische hirnoperationen bei sexuell devianten. *Hamburg* 2003; 1-201.
18. Lin D, Boyle MP, Dollar P, et al. Functional identification of an aggression locus in the mouse hypothalamus. *Nature* 2011;470:221-6.
19. Yang CF, Chiang MC, Gray DC, et al. Sexually dimorphic neurons in the ventromedial hypothalamus govern mating in both sexes and aggression in males. *Cell* 2013;153:896-909.
20. Franzini A, Broggi G, Cordella R, et al. Deep-brain stimulation for aggressive and disruptive behavior. *World Neurosurg* 2013; 80:S29 e11-4.
21. Torres CV, Sola RG, Pastor J, et al. Long-term results of posteromedial hypothalamic deep brain stimulation for patients with resistant aggressiveness. *J Neurosurg* 2013;119:277-87.
22. Krueger RB, Wechsler MH, Kaplan MS. Orchiectomy. In: Saleh FM, Grudzinskas AJ, Bradford JM, Brodsky DJ, editor. *Sex Offenders* Oxford: University Press;2009:171-188.
23. Alexander M, Gunn J, Cook DA, et al. Should a sexual offender be allowed castration? *BMJ* 1993;307:790-3.
24. Rada RT. Psychosurgery and the psychiatric implications of the Kaimowitz case. *Bull Am Acad Psychiatry Law* 1974;2:96-100.
25. Schuepbach WM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. *N Engl J Med* 2013;368:610-22.
26. Lewis CJ, Maier F, Horstkötter N, et al. Subjectively perceived personality and mood changes associated with subthalamic stimulation in patients with Parkinson's disease. *Psychol Med* 2015;45:73-85.